Title: Functional Electrical Stimulation Use in Trans-tibial Amputations

Clinical Trials.gov ID: NCT02931396

Protocol Date: 4/15/2018

Background

Transcutaneous electrical stimulation (TENS) is an alternate form of electrical stimulation that historically used high frequencies for pain relief (1) but is now also administered at very low frequencies (sensory level TENS, 2-10 Hz) (2) TENS propagates along smaller afferent sensory fibers specifically to override pain impulses. When very low frequencies are used, TENS specifically targets sensory nerve fibers and does not activate motor fibers; therefore, no discernible muscle contraction is produced (3). Electrical stimulation is currently used in many forms to facilitate changes in muscle action and performance. In clinical settings, electrical stimulation can be used for improving muscle strength, increasing range of motion, reducing edema, decreasing atrophy, healing tissue, and decreasing pain. Neuromuscular electrical stimulation (NMES), used interchangeably with electrical stimulation (ES), is typically provided at higher frequencies (20-50 Hz) expressly to produce muscle tetany and contraction that can be used for "functional" purposes and can be found in literature as early as 1964 (4). This combination is known as functional electrical stimulation (FES). FES is applied to peripheral nerves that control specific muscles or muscle groups (5). Types of FES may activate musculature to restore lost abilities such as standing or grasping following neurological damage from CVA or SCI. FES may also assist with some secondary problems of neurologic damage such as poor circulation or slow wound healing (6). There is a paucity of studies evaluating the use and efficacy of FES to treat edema, skin integrity and residual limb, and chronic or phantom pain in individuals with TTA whereas FES research has been widely conducted with persons with other medical conditions such as Spinal Cord Injury (SCI), Multiple Sclerosis (MS), and Cerebrovascular Accident (CVA) (6,7,8).

Most studies on FES have shown positive results when combining FES with activity (e.g. knee flexion/extension exercises, cycling etc.) (9). It is difficult to exercise a muscle that has been amputated and is partially intact. FES conditions the muscle similar to exercise. Our clinical experience has found improvements in knee function, socket fit, and reductions in pain with wearing FES alone. With this study, one of the main functional outcomes that we are investigating is knee extension. We plan to place the FES electrodes on the medial and lateral quadriceps muscles in hope to show positive changes in muscle strength and volume. The gastroc/ soleus and tibialis anterior muscles have been amputated and have a secondary insertion point, therefore they are difficult to strengthen by exercising. We would like to investigate the effects of the FES on these two muscles in hopes to decrease atrophy or increase muscle volume. Should we demonstrate that FES alone helps improve the outcome measures in this study; it could potentially be a highly practical, easy to use, cost effective treatment that can be done at home.

Objective: To determine if at-home FES use without prosthetic wear results in benefits to persons with unilateral, trans-tibial amputations (TTA) who are at least two years status post their amputation surgery.

Hypothesis 1: FES will increase knee extension strength in the residual limb
Hypothesis 2: FES will increase volume of the residual limb
Hypothesis 3: FES will decrease chronic and phantom pain of the residual limb
Hypothesis 4: In comparison to the control group, FES training will show greater increases in velocity, step length, and percentage in stance time on the amputated limb after training when compared to baseline as measured using the GaitRite System.

Study Design and Methods

Subjects will be recruited and randomized into two groups using a random block method at the end of the baseline visit. One group will receive the FES intervention and the other group will continue with their activities of daily living. The study consists of a baseline visit and four follow up visits at 4 weeks, 8 weeks, 12 weeks and one final visit three months from the 12 week visit or from the discontinuation of the FES. Outcome measures will be taken for both groups during these visits. Each visit is expected to take no more than two hours.

Following informed consent, it will be verified and documented that participants meet the inclusion/exclusion criteria. Most of the inclusion/exclusion criteria are self report, with the exception of the monofilament evaluation and the evaluation of voluntary muscle contraction. An investigator will administer the tests. For the sensory testing the participant will be asked to close their eyes and inform the investigator when they sense the pressure of the monofilament on their LE. In order to continue with the study procedures, the participant must be able to feel a minimum of 7 of the 10 areas tested. Participants will also be evaluated to determine if a voluntary muscle contraction is present. To do this the FES electrode pads will be placed on the participant and the investigator must be able to observe a muscle contraction in order to proceed. Any participants who do not meet the inclusion/exclusion criteria for the study will be withdrawn.

The following procedures and outcome measures will be obtained from a blinded (second) assessor at the baseline visit.

1. Residual knee extension strength will be tested using a standardized Biodex protocol and a custom attachment (System 3, Biodex Medical Systems, NY). The participant will practice first on the biodex machine with their intact limb.

2. The residual limb volume will be measured with the use of a hand held three-dimensional motion-tracking laser scanner system. Reflective markers will be placed on a sock over the residual limb located at the tibial tubercle, fibular head, and anterior distal tibia. Circumferential measurements of the residual limb will be taken with a tape measure. Longitudinal measurements of the residual limb will be taken with a straight ruler. Using a standard scale, participant's height and weight will be recorded.

3. The participant will complete a pain questionnaire that addresses both chronic and residual limb pain.

4. The participant will fill out the Prosthetics Evaluation Questionnaire (PEQ). This survey measures outcomes in regards to prosthesis function and prosthesis related quality of life.

5.Participants will be tested with the GaitRite motion analysis system (http://www.gaitrite.com/). Participants will perform a 10 meter walk test in one direction at a self-selected walking speed. Participants will repeat this 3 times with brief rest periods in between as needed. Velocity, step length and percentage of stance time will be collected.

Study participants who are randomized into the intervention group will be fitted with a portable commercially available surface FES device. A trained investigator, Sara Peterson, CPO, will fit the electrodes and explain the function of the FES device to the participant. The electrodes will be placed on the following locations: medial and lateral quadriceps, anterior tibialis (TA) and the gastrocnemius / soleus (GS) muscles on the residual limb. The FES settings will be individualized and optimized for eliciting muscle contraction of the residual limb while maintaining a comfortable level of stimulation. We will instruct participants on how to alternate the stimulation between the proximal knee (2 parts of the quadriceps) and the distal knee (TA and GS). Participants will be taught how to position the electrodes and how to operate the unit. They will be instructed to apply and wear the FES during a time of rest (non-active times of the day) and will be given extra sets of electrodes and batteries to use throughout the study. They will be provided with a pamphlet with simple instructions and photos on where and how to place, remove and store the electrodes. The instructions will include the wearing schedule and who to contact if they have questions.

We plan to use the recommended standard protocol settings in the product manual. We will start with the setting for the quadriceps muscles set at 300ms pulse width and 50Hz for the pulse rate. Channel 1 settings will be as follows: lag delay of 3 seconds, ramp up time of 3 seconds, on time of 12 seconds and ramp down of 2 seconds. Channel 2 settings will be as

follow: lag delay of 3 seconds, ramp up time of 2 seconds, on time of 9 seconds and ramp down of 1 second. For the smaller muscles of the gastroc/soleus and anterior tibialis muscles we will start with the setting of the 300ms pulse width and 35 Hz for the pulse rate. There will be no lag delay. Channel 1 settings will be as follows: ramp up time of 2 seconds, on time of 10 seconds and ramp down time of 2 seconds. Channel 2 settings will be as follows: ramp up time of 2 seconds, time on of 10 seconds and a ramp down for 2 seconds. The pulse rate and width will be increased at each visit per participant's comfort level.

We will record the settings at each visit and instruct the patient to not change the settings. The Continuum device locks the intensity increase buttons to prevent accidental increases in intensity. This safety feature is activated after 20 seconds of unchanged intensity.

Both study groups will be given daily logs to record daily prosthetic wearing times, changes in health, medications, activity, pain levels and FES use (the intervention group only).

Intervention group participants will be directed to use the FES for 15 contractions per muscle group (totally approximately 45 minutes) a minimum of three times per week for the next three months at home. We will set up a face-to-face visit with the FES participants at the end of the first week and call the FES participants every two weeks thereafter to check on compliance and address any issues with using the device. If the participant reports an ill-fitting prosthesis during the study, we will refer the participant to their local prosthetist for proper adjustments. If the prosthetic socket warrants replacement, the participant will be withdrawn from the FES intervention, we will perform the above mentioned outcome measures and continue to follow them until the 3 month final follow up visit.

At each follow up visit the log book entries will be collected and reviewed. A second investigator will inspect the residual limb and check the fit of the prosthetic socket, record residual limb knee extension strength on the Biodex machine, take anthropometric measurements (circumferences and lengths) of the residual limb with a tape measure and ruler, and scan the limb with the hand held three-dimensional motion-tracking laser scanner system. The participant will be asked to complete the pain questionnaire at all four followup visits and the Prosthetic Evaluation Questionnaire (PEQ) at the 12 weeks and 3 month followup visits.

For the isokinetic evaluation with the Biodex, the individuals will be positioned in the dynamometer, sitting with the trunk, pelvis and thigh stabilized by belts. The back of the chair will be inclined at an 85 degree angle and the rotational axis of the device will be aligned with the rotational axis of the knee joint, at the level of the lateral epicondyle of the femur. The lever arm was positioned parallel to the leg, with the support cushion modified for the amputee and positioned at the mid-calf. The test will be performed in a total range of motion of 110 degrees. The knees will be positioned in 60 degrees of flexion to start.

Muscle performance will be evaluated at angular velocity of 60, during isokinetic quadriceps contractions. To assure familiarization with the procedures the participant will have two practice submaximal trial repetitions set at the velocity of 60 and one practice trial. The test will consist of 5 repetitions at 60/s. There will be a 60 second interval between repetitions tested. During evaluation, the participants will be verbally instructed to move the lever of the dynamometer as fast and as powerfully as possible, trying to produce a maximum torque. Any complaints reported by the participant will be recorded in the comment section and, if necessary, the test will be stopped. Using the same seat set up, muscle performance will be evaluated during static concentric (isometric) quadriceps extension contractions. The lever arm will be positioned at 60 degrees of knee flexion, with the support cushion modified for the amputee and positioned at mid calf. The participant will have one practice submaximal trial contraction. The test will consist of three contractions for five seconds each. There will be a 60 second interval between each test. During evaluation, the participants will be verbally instructed to move the lever of the dynamometer as powerfully as possible, trying to produce a maximum torque. Any complaints reported by the participant will be recorded in the comment section and, if necessary, the test will be stopped

At the 12 week visit, the intervention group participants will return the FES device. They will be followed up with one final visit 3 months after the FES device is returned.

At the end of the study, should the study find the FES intervention is beneficial, we will offer the control group the same intervention. It will be optional per participant request.

If a subject misses the last visit or is dropped from the study for a reason not related to the study and or beyond our control, we will ask to set up a follow up visit, face to face, or a phone interview to allow us to gather end result information and complete the data analysis.

Eligibility Criteria

Inclusion Criteria:
The inclusions include both men and women over the age of 18 years old. Participants are unilateral trans-tibial amputees with a minimum of a 4" residual limb. This length of amputation was chosen to provide for adequate surface area for the electrodes. The participants must be a minimum of one year postoperative to insure proper healing of the limb has occurred. The participants must have chronic limb pain and have had no prior experience in using TENS or FES. Participants must also demonstrate the ability to voluntary elicit a muscle contraction.

Exclusion Criteria:
The exclusion criteria include having a cardiac condition, such as hypertension, congestive heart failure, etc. The exclusions will be subjects who have a pacemaker and have impaired sensation measured by a monofilament test (unable to feel a minimum of 7/10 areas tested). The use of FES may interfere with a pacemaker and is not suggested for people who have a pacemaker. People with insensate skin and or neuropathy may lead to inappropriate threshold tolerance to the FES. Also, participants with a BMI greater than 42 kg/m2 will be excluded as the FES does not work effectively with excessive adipose tissue.

Statistical Plan
Descriptive statistics will be computed and variables will be assessed for normality. Nonparametric tests will be performed in the event the data are not normal. An unpaired t-test or chi-square test depending on the type of variable will be used to compare the subject demographic variables (e.g. age, level of amputation, gender, etc.) between groups. A mixed model repeated measures ANOVA will be used to compare the outcome measures between groups and overtime. Compliance with the FES (e.g. average number of hours of use per week) will be entered as a covariate. We will also use correlation statistics (Pearson or Spearman) to examine the relationship between amount of FES used and changes in the dependent variables. Should significant main and interaction effect differences be found ($p < 0.05$), post-hoc analyses will be used to examine the differences in variables across the groups and time points. If the data fail to be normally distributed the Friedman test will be run.